

10/650,174 filed 08/28/2003  
Parce et al.  
Reply to Office Action of 05/19/2006

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**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (currently amended) A method of detecting a binding activity, the method comprising:  
detecting a detectable signal that indicates an initial concentration of at least one first component or set of first components prior to entry of the at least one first component or the set of first components into a first channel;  
flowing the at least one first component or ~~a~~ the set of first components through a ~~the~~ first channel concomitant with at least one second component or a set of second components ~~through the first channel~~, wherein the at least one first component or the set of first components diffuses more rapidly in solution than the at least one second component or the set of second components, and wherein the first channel comprises a mixing longitudinal segment, wherein the at least one first component or the set of first components diffuses substantially across the first channel in the mixing longitudinal segment, and wherein the at least one second component or the set of second components diffuses less than substantially across the first channel in the mixing longitudinal segment, wherein the at least one second component or the set of second components binds to the at least one first component or the set of first components; and;  
detecting a detectable signal that indicates a final concentration of the at least one first component or the set of first components that remains unbound after exiting from the first channel, thereby detecting the binding activity.

2. (canceled)

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3. (original) The method of claim 1, wherein the at least one first component or the set of first components is at least one ligand selected from one or more of: an antigen, a set of antigens, a protein, a set of proteins, a peptide, a set of peptides, a lipid, a set of lipids, a carbohydrate, a set of carbohydrates, an inorganic molecule, a set of inorganic molecules, an organic molecule, a set of organic molecules, a drug, a set of drugs, a receptor ligand, a set of receptor ligands, an antibody, a set of antibodies, a neurotransmitter, a set of neurotransmitters, a cytokine, a set of cytokines, a chemokine, a set of chemokines, a hormone and a set of hormones.

4. (original) The method of claim 1, wherein the binding activity is detected at a temperature in the range of from about 10 to about 40°C.

5. (original) The method of claim 1, wherein the binding activity is detected at a temperature of about 25°C.

6. (original) The method of claim 1, wherein the binding activity is detected at a temperature of about 37°C.

7. (original) The method of claim 1, wherein the at least one first component or the set of first components diffuses in the range of from about 1.5 to about 100 times faster in solution than the at least one second component or the set of second components.

8. (original) The method of claim 1, wherein the at least one first component or the set of first components diffuses about 50 times faster in solution than the at least one second component or the set of second components.

9. (original) The method of claim 1, wherein an initial concentration of the at least one first component or the set of first components prior to entry into the first channel is in the range of from about 1 nM to about 1 mM.

10. (original) The method of claim 1, wherein an initial concentration of the at least one first component or the set of first components prior to entry into the first channel is about 10  $\mu$ M.

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11. (original) The method of claim 1, wherein the at least one first component or the set of first components comprises a molecular weight in the range of from about 200 to about 1000 daltons.

12. (original) The method of claim 1, wherein the at least one first component or the set of first components comprises a molecular weight of about 400 daltons.

13. (original) The method of claim 1, wherein the at least one first component or the set of first components comprises a diffusional coefficient in the range of from about  $10^{-12}$  to about  $10^{-4} \text{ cm}^2 \text{ s}^{-1}$ .

14. (original) The method of claim 1, wherein the at least one first component or the set of first components comprises a diffusional coefficient of about  $10^{-6} \text{ cm}^2 \text{ s}^{-1}$ .

15. (original) The method of claim 1, wherein the at least one second component or the set of second components comprises one or more of: an enzyme, a receptor, a cell, or a nucleic acid.

16. (original) The method of claim 1, wherein the at least one second component or the set of second components is an enzyme having a concentration in the range of from about 1 nM to about 1 mM.

17. (original) The method of claim 1, wherein the at least one second component or the set of second components is an enzyme having a concentration of about 10  $\mu\text{M}$ .

18. (original) The method of claim 1, wherein the at least one second component or the set of second components is an enzyme that comprises a molecular weight in the range of from about 10 to about 200 kilodaltons.

19. (original) The method of claim 1, wherein the at least one second component or the set of second components is an enzyme that comprises a molecular weight of about 30 kilodaltons.

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20. (original) The method of claim 1, wherein the at least one first component or the set of first components and the at least one second component or the set of second components are flowed using one or more fluid direction components comprising one or more of: a fluid pressure force modulator, an electrokinetic force modulator, a capillary force modulator, and a fluid wicking element.

21. (original) The method of claim 1, further comprising the step of flowing the at least one first component or the set of first components through the first channel, thereby providing a positive control for detecting the detectable signal.

22. (canceled)

23. (original) The method of claim 1, wherein the first channel is a microchannel.

24. (original) The method of claim 1, the method comprising concomitantly flowing at least one modulator into contact with the at least one second component or the set of second components in the first channel, wherein the at least one modulator modulates the binding of the at least one second component or the set of second components to the at least one first component or the set of first components.

25. (original) The method of claim 24, wherein the at least one modulator inhibits the binding of the at least one second component or the set of second components to the at least one first component or the set of first components.

26. (original) The method of claim 24, wherein the detected binding activity provides an indication of one or more of: the binding activity of the at least one second component or the set of second components and an ability of the at least one modulator to modulate the binding activity of the at least one second component or the set of second components.

27. (original) The method of claim 1, wherein the detectable signals are selected from: a refractive index, a cellular activity, a light emission, a change in absorbance, a change in fluorescence, an absorbance, a fluorescence, a color shift, a fluorescence resonance energy transfer, a radioactive emission, a change in pH, a change in temperature, and a change in mass.

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28. (canceled)

29. (new) A method of detecting a binding activity, the method comprising:

flowing the at least one first component or the set of first components through the first channel concomitant with at least one second component or a set of second components, wherein the at least one first component or the set of first components diffuses more rapidly in solution than the at least one second component or the set of second components, and wherein the first channel comprises a mixing longitudinal segment, wherein the at least one first component or the set of first components diffuses substantially across the first channel in the mixing longitudinal segment, and wherein the at least one second component or the set of second components diffuses less than substantially across the first channel in the mixing longitudinal segment, wherein the at least one second component or the set of second components binds to the at least one first component or the set of first components;

detecting a detectable signal that indicates a final concentration of the at least one first component or the set of first components that remains unbound after exiting from the first channel, thereby detecting the binding activity; and

flowing the at least one second component or the set of second components through the first channel, thereby providing a negative control for detecting the detectable signal.